Remarks

Applicants appreciate and thank the Examiner and her supervisors for the Examiner Interview conducted on January 31, 2006. The Applicants have received the Interview summary and in response, indicate that in view of the interview, the amendments presented herein have been made to clarify the invention.

Claims 2-9, 12-17, 49-57 and 60-63 are pending. Claims 2-9 and 13-49 have been amended. Claim 12 has been canceled. Claims 70 and 71 are new. Each of the Examiner's rejections are addressed below.

Claim Rejection Under 35 USC §112

The Examiner has rejected claims 2,3, 12-14, 49-51 and 60 as failing to comply with the Written Description requirement, particularly with respect to the phrase "microorganism" and "compound",

It is respectfully pointed out that the essence of the invention is to provide microorganisms which are rendered non-pathogenic by the covalent attachment of surface proteins with reactive functional groups and in which the nuclear components are substantially intact. These microorganisms can serve as positive controls in detection methods based on nucleic acid amplification techniques.

Thus, with respect to the phrase "microorganism", Applicants submit that what Applicants have described are purified microorganisms rendered non-pathogenic by covalent bonding of surface proteins with reactive groups and yet amenable to nucleic acid amplification. The term "microorganism" is well understood in the art and is further described on page 5 line 23 through page 6, line 13. An exemplary list of microorganism is provided on page 6, lines 5-13. Exemplary data is provided for three viruses, HIV1, Hepatitis B and Bovine Viral Diarrhea Virus. Further, because it is also well recognized that all microorganisms express surface proteins, based on the description provided herein Applicants assert that it is well within the purview of those skilled in the art to apply this invention to other microorganisms and that one skilled in the art would consider this description to apply to other microorganisms.

With respect to the phrase "compound", it is respectfully pointed out that an extensive list of reactive groups is provided in the bridging paragraph between pages 7 and 8. Further, a

description of compounds is present on page 8, line 8 to page 9, line 11, and continues on pages 9-13.

The Examiner also contends that the phrase "surface proteins" is not defined by any names or structure. However, it is respectfully pointed out that the identity of the surface proteins is not critical to the invention. What is important is that the reactive groups covalently link the surface proteins so as to render the microorganisms non-pathogenic. Therefore Applicants assert that specific identification of the nature of the surface proteins is not necessary.

The Examiner also contends that the term "covalent attachment" would be understood to extend to any known prior art HIV cell or tissue fixative solution containing formaldehyde. Further, the Examiner also contends that the phrase "liquid matrix ...suitable for lyophilization" extends to any organic compound known in the prior art. Applicants agree that any solution containing a chemical capable of providing reactive groups as discussed on page 8, line 8 to page 9, line 11 would be capable of covalently attaching the surface proteins. However, again, the critical element of the invention is not the knowledge of these reactive group, but the application of these reactive groups in such a way as to render the microorganism non-pathogenic while keeping the nuclear components intact. Applicants assert that compositions comprising such purified microorganisms in which the nuclear components are substantially intact and in which the microorganisms are suspended in a liquid matrix comprising a biological fluid after purification, are not known in the prior art.

The Examiner further asserts that claiming the genus is improper because there is no distinguishing feature for the surface proteins, the virus and the compound. As discussed above, the identity of the surface proteins is not critical and therefore not necessary to the invention. With respect to the virus, Applicants have provided data for HIV (Examples 1-6), Hepatitis B (Example 7) and for Bovine Viral diarrhea Virus (BVDV). Having provided examples of three different viruses, an exemplary list of microorganisms and a detailed basis and description for the inactivation of the microorganism, Applicants assert that the genus of virus as well as microorganism meets the written description requirement. With respect to the "compound" Applicants assert that a sufficiently detailed description of the reactive groups has been provided thereby providing the distinguishing features of the reactive groups.

Based on the above arguments, Applicants believe the claims are in conformance with the Written Description requirement.

Claim Rejection Under 35 USC §102

The Examiner has rejected claims 2-4, 12-15, 49-52 and 60-61 as being anticipated by Davison et al. (1996). Applicants respectfully request reconsideration for the following reasons. Applicants have amended claim 2 to emphasize that the composition comprises purified microorganisms in a liquid matrix comprising a biological fluid or a synthetic biological fluid such that the composition can be used as a positive amplification control and the microorganism is purified prior to adding to the liquid matrix.

Davison et al. disclose that HIV-1 DNA can be identified in formalin fixed tissues. In this reference, formalin fixed tissues were dewaxed, and then treated with xylene and ethanol. DNA was then prepared from it and then used for amplification. It should be noted that in the case of HIV, a RNA virus, the nucleic acid in the microorganism is RNA. When it is reverse transcribed in a cell, corresponding DNA is produced. The cited reference of Davison described the extraction of such a reverse transcribed (by the infected cell) DNA. Nowhere does Davison provide purified a purified virus which has been rendered non-pathogenic by covalent bonding of the surface proteins with reactive groups and in which the nucleic acids are intact so as to be amenable to amplification. Since this reference does not provide all the elements of claim 2 and its dependent claims, it cannot be deemed to anticipate the claims.

During the Examiner interview, the Examiners also identified the reference of Grovit-Ferbas (2000). Because this reference has not been made of record yet, Applicants are providing that on the attached IDS. With respect to this reference, Applicants respectfully point out this reference does not describe the suspension of the purified microorganism in the liquid matrix comprising a biological fluid or a simulated biological fluid as required by the amended claim 2. This is important for the composition of claim 1 to serve as a positive control in nucleic acid amplification reactions where the test samples are typically present in biological fluids. Because the reference of Grovit-Ferbas does not provide a composition comprising a purified microorganism which is suspended in liquid matrix comprising a biological fluid, it cannot be deemed to anticipate the present claims.

Applicants respectfully point out that the composition of the present invention has been successfully used as a positive control material in amplification methods for the detection of microorganisms. The reason this composition can serve as a reliable positive control material is because the microorganisms are purified, their surface proteins covalently modified, and then suspended in liquid matrix comprising a biological fluid such that the composition can be used in parallel with a test sample for amplification reactions.

Applicants emphasize that the use of positive controls in nucleic acid amplification based methods for detecting the presence of microorganisms is critical for accurate results. The present composition can be used for this purpose because of the purification and suspension in a liquid matrix comprising a biological fluid or a simulated biological fluid. Further, the composition as recited in claim 1, can be stored as 2-8 C (page 14, lines 29-30) and yet maintain its ability to serve as a positive control material. None of these features are identified or even sought in the cited references. Therefore, Applicants assert that the cited references do not provide a composition as recited in the amended claims.

Conclusion

Based on the amendments and the arguments presented herein, Applicants believe claims 2-9, 12-17, 49-57, 60-63 and 70-71 are now in a condition for allowance and therefore request the Examiner to allow these claims.

Applicants hereby request a three-month extension for filing of this response. A check for $1020.00 is enclosed. If any additional fee is due, it may be charged to Deposit Account no. 08-2442.

Respectfully submitted,

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